REMARKS

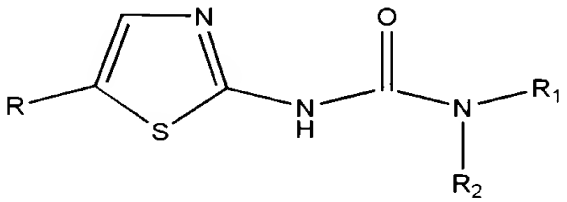
Claims 1-4, 6-12 and 14-21 were pending prior to this amendment. By an Amendment filed November 27,2002 claims 1, 6, 7, 8, 10 and 17 were amended to add thereto a proviso as follows: "with the proviso that R_1 is not a C_1-C_6 alkyl having 1-6 oxo groups when R is a bromine or iodine atom." This proviso was added to distinguish the Islip reference that was applied as a 35 USC § 102 (b) basis for the rejection of claims 1-4, 6-8, 10, 14 and 16. The next and final Office Action then stated a new rejection of all pending claims under 35 USC § 112, first paragraph, on grounds that the so added proviso was not supported by the written specification. Also this Office Action cited a new reference, Wood et al., as a 35 USC § 102 (e) basis for the rejection of claims 1-4, 6-8, and 14-21. No art based rejection of dependent claims 9, 11, or 12 has ever been stated.

The amendments here offered for entry into this case delete the proviso from the claims (claims 1, 6-8, 10 and 17) in order to eliminate the 35 USC § 112, first paragraph, rejection to which the proviso gave rise. Dependent claims 9, 11 and 12 which were never rejected for art reasons are amended to independent form to place them in condition for allowance. Claim 21 is amended to recite its dependency from claim 7 to moot its rejection under 35 USC § 112, second paragraph. At a minimum entry of the requested amendments will simplify the issues on appeal, and entry is requested.

As to the so amended claims, reconsideration of the rejections over Islip and Wood is requested in light of the remarks which follow.

The Islip Reference

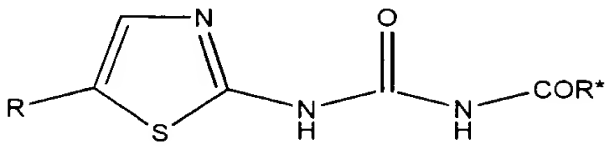
All of the claims define and are limited to a 2-amino-1,3-thiazole derivative of formula (I)



(I)

The specification allows R_1 of the claims to be an "optionally further substituted group" selected from: i) straight or branched "C_1-C_6 alkyl"; . . . .

Islip is applied for a § 102 rejection of our claims 1-4, 6-8, 10, 14 and 16 because Islip discloses the following compound:



Islip

The claimed R position may be halogen and Islip may be Br or I at the claimed R position. The claimed R_2 position may be hydrogen and Islip is hydrogen at the claimed R_2 position. Islip at the claimed R_1 position is an acyl group so the question is whether the claim defined R_1 group is allowed by the specification to read upon an acyl group.

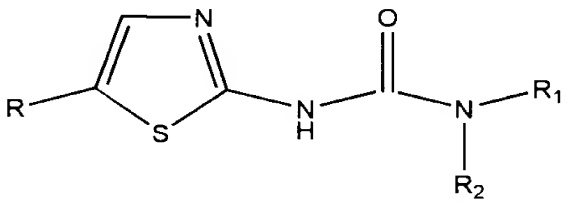
No where does the specification or claims state that R_1 may be an "acyl" group, a/k/a an "alkanoyl" or a "carbonyl" group. An "acyl" group is an organic radical derived from an organic acid by the removal of the hydroxyl group (Hackh's Chemical Dictionary, © 1969, page 16 – copy enclosed). The claims allow for the R_1 group to be a C_{1-6} alkyl which may contain an "optionally further substituted group" at "the free positions" (specification at page 10, line 35). To achieve the acyl group of Islip the Examiner hypothecates as an "optionally further substituted group" an oxo substitution of the first carbon atom of the C_{1-6} alkyl. However one skilled in the art would not consider such a structure to be an oxo substituted C_{1-6} alkyl but instead would consider such a structure to be a member of the acyl/akanoyl/carbonyl group. Accordingly, as respects a C_{1-6} alkyl "the free positions" (page 10, line 35) open to oxo substitution are only at the 2-6 carbon atoms for only in this way is the nature of the group as a claimed "alkyl" preserved. So the Examiner not only reads the specification wrongly (a 1-oxo-alkyl is an "acyl" and not an "alkyl") the Examiner violates the specification that says oxo substitution may only occur at "the free positions" (page 10, line 35) of the "alkyl" which are only the 2-6 carbon position if the structure is to maintain its claimed "alkyl" identity. One skilled in the art, even if considering an oxo substituted C_1-C_6 "alkyl", would not consider oxo substitution at the first carbon thereof since this product radical (-COR) would be recognized in the art to be an acyl/akanoyl/carbonyl group and not an 1-oxo alkyl. Since the claims by their express language do not allow for the R_1 group to be an acyl/akanoyl/carbonyl group, it is error for the Examiner to go against the rules of nomenclature and artificially construct an

acyl group from an oxo substituted "alkyl" by placing the proposed oxo substituent at the first carbon position to convert it into an "acyl" group that the claims do not name.

The rejection of claims 1-4, 6-8, 10, 14, and 16 over Islip should be withdrawn.

The Wood Reference

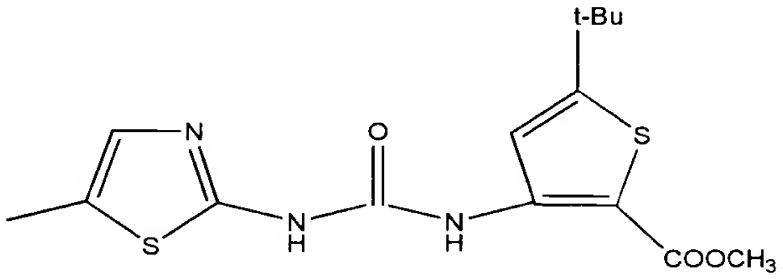
All of the claims define and are limited to a 2-amino-1,3-thiazole derivative of formula (I)



(I)

The specification allows R_1 of the claims to be an "optionally further substituted group" selected from: ii) 5 to 7 membered heterocycle ring.

Wood is applied for a § 102 rejection of our claims 1-4, 6-8, and 14-21 because Wood discloses the following compound:



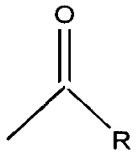
Wood et al

The claimed R position may be methyl and Wood is methyl at the claimed R position. The claimed R_2 position may be hydrogen and Wood is hydrogen at the claimed R_2 position. Wood at the claimed R_1 position is a 5-alkyl 2-ester substituted thiophene group so the question is whether the claim defined R_1 group is allowed by the specification to read upon an ester substituted thiophene group. The specification allows the R_1 group to be a thiophene group but the specification does not allow for an "optionally further substituted group" on the thiophene to be an ester group.

Without so stating, the Examiner apparently believes that the passage at page 10, line 33-page 11, line 21 of the specification allows for a substitutent on the "5 to 7 member

heterocycle ring" to be a carboxylic acid methyl ester as is present in the 5-member heterocycle ring (thiophene) of the compound at the top of column 4 of Wood. However, on this point the Examiner is wrong.

The "carboxy" at page 10, line 37 does not allow for a carboxylic acid ester since a carboxy group is of the structure –COOH, it is a free acid and not an ester. ("Carboxy. Carboxyl. Carboxyl. . . . The acidic –COOH group." Hackh's Chemical Dictionary, © 1969, page 134 – copy enclosed) Nor does the "carbony groups" of page 11, lines 11-14 of the specification allow for a carboxylic acid ester since a carbonyl group is of the structure:



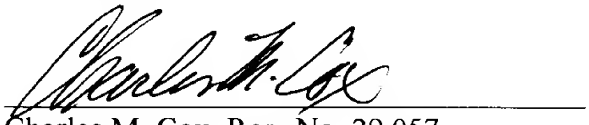
and in essence is an acyl group. (Carbonyl. The radical =CO. Hackh's Chemical Dictionary, © 1969, page 133 – copy enclosed) We also note from the passage at page 11, lines 19-25 of the specification that the substitutents of the R_1 group may themselves be "optionally further substituted as set forth above" with examples thereof "given below." The Examiner may cite this passage for the proposition that the "5 to 7 member heterocycle ring" is first substituted with "carboxy" (page 10, line 37) and this carboxy group is further substituted with "alkyl" (page 10, line 37) to yield a carboxylic acid ester. This argument, if it is made, would violate the specification teaching that the substitution and/or further substitutions of a substituent are allowed only at "the free positions" (page 10, line 35) which means a carbon atom position that bears one or more substitutable hydrogen atoms. Hence, the conversion of a first carboxyl substitutent (–COOH) into a ester substitutent (–COOR) is not permitted by the specification since the hydroxyl (-OH) of the carboxyl substitutent is not a "free position." The Examiner is also invited to review the 238 named compound examples at pages 14-25 of the specification to see that there are no examples of a carboxylic acid ester substitutent either as a first generation substitutent or as resulting from a further substitution of a first generation carboxyl group with an alkyl.

The rejection of claims 1-4, 6-8, and 14-21 over Wood should be withdrawn.

CONCLUSION

For the foregoing reasons, Applicant submits that with the proposed amendments claims 1-21 stand in condition for allowance. Withdrawal of the objections and rejections and allowance of these claims is respectfully requested.

Respectfully submitted,



Charles M. Cox, Reg. No. 29,057

Date: March 21, 2003

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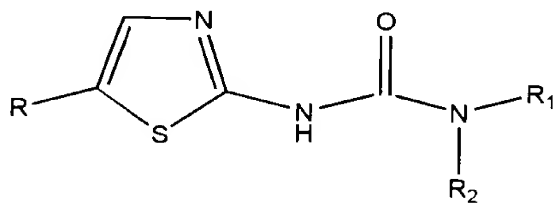
ATTACHMENT A

Marked-Up Version Of Amended Claims (as of 3/21/03)

--1. (Twice Amended) A method of treating, arresting, alleviating, or reducing cell proliferative disorders associated with an altered cell dependent kinase activity in a patient comprising

administering a 2-ureido-1,3-thiazole derivative of formula (I)



(I)

wherein

R is a halogen atom, a nitro group, an optionally substituted amino group or it is a group, optionally further substituted, selected from:

i) straight or branched C_1-C_6 alkyl;

ii) C_3-C_6 cycloalkyl;

iii) aryl or arylalkyl with from 1 to 6 carbon atoms within the straight or branched alkyl chain;

R_1 is an optionally further substituted group selected from:

i) straight or branched C_1-C_6;

ii) 3 to 6 membered carbocycle or 5 to 7 membered heterocycle ring;

iii) aryl or arylcarbonyl;

iv) arylalkyl with from 1 to 6 carbon atoms within the straight or branched alkyl chain **[, with the proviso that R_1 is not a C_1-C_6 alkyl having 1-6 oxo groups when R is a bromine or iodine atom]**;

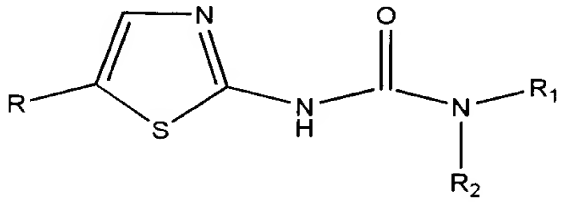
R_1 is hydrogen, a straight or branched C_1-C_4 alkyl or C_2-C_4 alkenyl or alkynyl group; or, taken together with the nitrogen atom to which they are bonded,

R_1 and R_2 form a substituted or unsubstituted group selected from:

i) an optionally benzocondensed or bridged 5 to 7 membered heterocycle; or

ii) a 9 to 11 membered spiro-heterocyclic compound; or a pharmaceutically acceptable salt thereof to the patient.

6. (Twice Amended) A 2-ureido- 1,3-thiazole derivative of formula (I)



(I)

wherein

R is a halogen atom, a nitro group, an optionally substituted amino group or it is a group, optionally further substituted, selected from:

i) straight or branched C_1-C_6 alkyl;

ii) C_3-C_6 cycloalkyl;

iii) aryl or arylalkyl with from 1 to 6 carbon atoms within the straight or branched alkyl chain;

R_1 is an optionally further substituted group selected from:

i) straight or branched C_1-C_6 alkyl;

ii) 3 to 6 membered carbocycle or 5 to 7 membered heterocycle ring;

iii) aryl or arylcarbonyl;

iv) arylalkyl with from 1 to 6 carbon atoms within the straight or branched alkyl chain **[, with the proviso that R_1 is not a C_1-C_6 alkyl having 1-6 oxo groups when R is a bromine or iodine atom]**;

R_2 is hydrogen, a straight or branched C_1-C_4 alkyl or C_2-C_4 alkenyl or alkynyl group; or, taken together with the nitrogen atom to which they are bonded,

R_1 and R_2 form a substituted or unsubstituted group selected from:

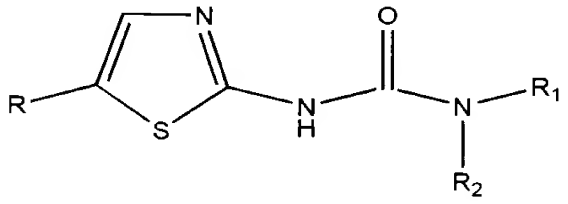
i) an optionally benzocondensed or bridged 5 to 7 membered heterocycle; or

ii) a 9 to 11 membered spiro-heterocyclic compound; or a pharmaceutically acceptable salt thereof; [for use as a medicament]; provided that:

a) when R is a chlorine atom and R_2 is hydrogen, then R_1 is not methyl, phenyl or trifluoromethylphenyl; and

b) when R is methyl and R_2 is hydrogen, then R_1 is not 4-(5-oxazolyl)phenyl.

7. (Twice Amended) A 2-amino-1,3-thiazole derivative of formula (I)



(I)

wherein

R is a halogen atom, a nitro group, an optionally substituted amino group or it is a group, optionally further substituted, selected from:

i) straight or branched C_1-C_6 alkyl;

ii) C_3-C_6 cycloalkyl;

iii) aryl or arylalkyl with from 1 to 6 carbon atoms within the straight or branched alkyl chain;

R_1 is an optionally further substituted group selected from:

i) straight or branched C_1-C_6 alkyl;

ii) 3 to 6 membered carbocycle or 5 to 7 membered heterocycle ring;

iii) aryl or arylcarbonyl;

iv) arylalkyl with from 1 to 6 carbon atoms within the straight or branched alkyl chain **[, with the proviso that R_1 is not a C_1-C_6 alkyl having 1-6 oxo groups when R is a bromine or iodine atom]**;

R_2 is hydrogen, a straight or branched C_1-C_4 alkyl or C_2-C_4 alkenyl or alkynyl group; or, taken together with the nitrogen atom to which they are bonded,

R_1 and R_2 form a substituted or unsubstituted group selected from:

i) an optionally benzocondensed or bridged 5 to 7 membered heterocycle; or

ii) a 9 to 11 membered spiro-heterocyclic compound; or a pharmaceutically acceptable salt thereof, provided that:

a) when R is chlorine or bromine and R_2 is hydrogen, then R_1 is not unsubstituted C_1-C_3 alkyl, phenyl, trifluoromethylphenyl or an optionally substituted phenylcarbonyl;

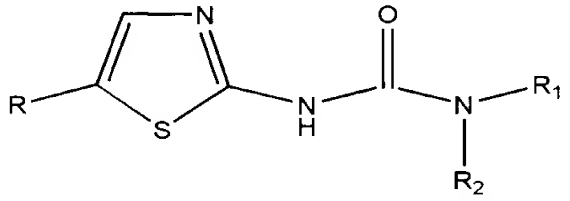
b) when R is methyl and R_2 is hydrogen, then R_1 is not methyl, phenyl or 4-(5-oxazolyl)phenyl;

c) when R is nitrophenyl and R_2 is hydrogen, then R_1 is not haloalkyl;

d) when R is bromine or chlorine, then R_1 and R_2 are not both methyl groups.

8. (Twice Amended) The derivative according to Claim 7, wherein R is a halogen atom, a straight or branched C_1-C_4 alkyl group, a phenyl group, a cycloalkyl group; R_2 is hydrogen and R_1 is an optionally substituted group selected from alkyl, aryl or arylakyl **[; with the proviso that R_1 is not a C_1-C_6 alkyl having 1-6 oxo groups when R is a bromine or iodine atom]**.

9. (Amended) **[The derivative according to Claim 8, wherein]** A 2-amino-1,3-thiazole derivative of formula (I)



(I)

wherein

R is bromine, chlorine, a straight or branched C_1-C_4 alkyl group, a phenyl group, a cycloalkyl group; R_2 is hydrogen and R_1 is an optionally substituted aryl or an arylalkyl or heterocyclyl-alkyl group having from 1 to 4 carbon atoms within the alkyl chain.

10. (Amended) The derivative according to Claim 7, wherein

R is a halogen atom or is selected from the group consisting of nitro, amino, alkylamino, hydroxyalkylamino, arylamino, C_3-C_6 cycloalkyl, straight or branched C_1-C_6 alkyl optionally substituted by hydroxy, alkylthio, alkoxy, amino, alkylamino, alkoxycarbonylalkylamino, alkylcarbonyl, alkylsulfonyl, alkoxycarbonyl, carboxy, and aryl each optionally substituted by one or more hydroxy, halogen, nitro, alkoxy, aryloxy, alkylthio, arylthio, amino, alkylamino, dialkylamino, N-alkyl-piperazinyl, 4- morpholinyl, arylamino, cyano, alkyl, phenyl, aminosulfonyl, aminocarbonyl, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl or carboxy, or R is an aryl group optionally substituted by one or more hydroxy, halogen, nitro, alkoxy, aryloxy, alkylthio, arylthio, amino, alkylamino, dialkylamino, N-alkyl-piperazinyl, 4-morpholinyl, arylamino, cyano, alkyl, phenyl, aminosulphonyl, aminocarbonyl, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl or carboxy;

R_1 is a straight or branched C_1-C_6 alkyl group or an aryl group, each optionally substituted as above reported for R **[, with the proviso that R_1 is not a C_1-C_6 alkyl having 1-6 oxo groups when R is a bromine or iodine atom]**;

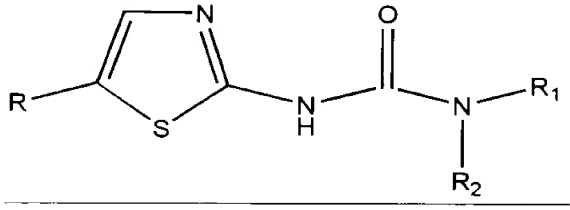
R_2 is a hydrogen atom; and pharmaceutically acceptable salts thereof provided that:

a) when R is chlorine or bromine then R_1 is not unsubstituted C_1-C_3 alkyl, phenyl, trifluoromethylphenyl or an optionally substituted phenylcarbonyl;

b) when R is methyl then R_1 is not methyl, phenyl or 4-(5oxazolyl)phenyl;

c) when R is nitrophenyl then R_1 is not haloalkyl.

11. (Amended) **[The derivative according to Claim 7, wherein]** A 2-amino-1,3-thiazole derivative of formula (I)



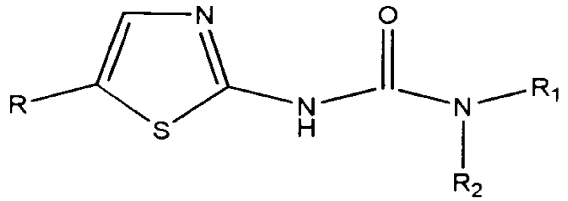
(I)

wherein

R is a straight or branched C_1-C_6 alkyl group and, together with the nitrogen atom to which they are bonded, R_1 and R_2 form a substituted or unsubstituted, optionally

benzocondensed or bridged 5 to 7 membered heterocycle, or a 9 to 11 membered spiro-heterocycle.

12. (Amended) **[The derivative according to Claim 7, wherein]** A 2-amino-1,3-thiazole derivative of formula (I)



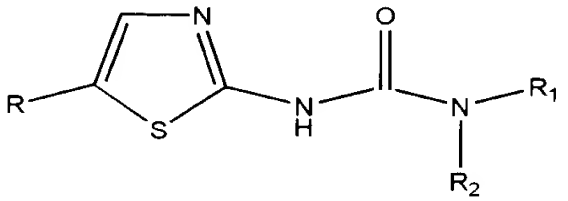
(I)

wherein

R is a straight or branched C_1-C_6 alkyl group; R_2 is a straight or branched C_1-C_4 alkyl or C_2-C_4 alkenyl or alkynyl group and R_1 is an aryl or arylalkyl group with from 1 to 4 carbon atoms within the straight or branched alkyl chain.

17. (Twice Amended) A method of treating, arresting, alleviating, or reducing tumor angiogenesis and metastasis inhibition in a patient, comprising

administering a 2-ureido-1,3-thiazole derivative of formula (I)



(I)

wherein

R is a halogen atom, a nitro group, an optionally substituted amino group or it is a group, optionally further substituted, selected from:

i) straight or branched C_1-C_6 alkyl;

ii.) C_3-C_6 cycloalkyl;

iii) aryl or arylalkyl with from 1 to 6 carbon atoms within the straight or branched alkyl chain;

R_1 is an optionally further substituted group selected from:

i) straight or branched C_1-C_6

ii) 3 to 6 membered carbocycle or 5 to 7 membered heterocycle ring;

iii) aryl or arylcarbonyl;

iv) arylalkyl with from 1 to 6 carbon atoms within the straight or branched alkyl chain **[, with the proviso that R_1 is not a C_1-C_6 alkyl having 1-6 oxo groups when R is a bromine or iodine atom]**;

R_2 is hydrogen, a straight or branched C_1-C_4 alkyl or C_2-C_4 alkenyl or alkynyl group; or, taken together with the nitrogen atom to which they are bonded,

R_1 and R_2 form a substituted or unsubstituted group selected from:

i) an optionally benzocondensed or bridged 5 to 7 membered heterocycle; or

ii) a 9 to 11 membered spiro-heterocyclic compound; or a pharmaceutically acceptable salt thereof to the patient.

21. (Amended) The derivative according to Claim **[17]** 7, wherein the optionally substituted group of R, R_1, and R_2 of formula (I) is optionally substituted with at least one member selected from the group consisting of halogen, nitro, oxo, carboxy, cyano, alkyl, perfluorinated alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocyclyl, amino, alkylamino, alkoxycarbonylalkylamino, dialkylamino, arylamino, diarylamino, alkylsulfonylamino, arylureido, carbonylamino groups, formylamino, alkylcarbonylamino, alkenylcarbonylamino, arylcarbonylamino, alkoxycarbonylamino, oxygen-substituted oximes, alkoxycarbonylalkoxyimino, alkoxyimino, hydroxy, alkoxy, aryloxy, alkylcarbonyloxy, arylcarbonyloxy, cycloalkenyloxy, carbonyl, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, cycloalkyloxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl,, alkylthio, arylthio, alkylsulphonyl, arylsulphonyl, alkylsulphinyl, arylsulphinyl, arylsulphonyloxy, aminosulfonyl, alkylaminosulphonyl, and dialkylaminosulphonyl.